



Docket No. IVD 941-2

#7
4-10-03
S. J. Lome

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Duchaussoy et al.

Serial No.: 09/686,373

Filing Date: October 11, 2000

Group Art Unit: 1623

Examiner: Fonda, Kathleen Kahler

FOR: Synthetic Polysaccharides, Methods For
Preparing Same and Pharmaceutical Compositions
Containing Said Polysaccharides

Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

CERTIFICATE UNDER 37 C.F.R. 1.8(a)

I hereby certify that this correspondence is being
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Genevieve A. Shier
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RESPONSE AFTER FINAL

This is responsive to the Office Action mailed October 1, 2002, setting a three-month shortened statutory period for response expiring January 1, 2003. Pursuant to the Petition for Extension of Time under 37 C.F.R. 1.136(a) submitted herewith, the period for response is extended three months to April 1, 2003. This response and the accompanying Notice of Appeal are therefore timely filed.

Claims 1-21 and 25-29, all the claims in the application, are rejected under 35 U.S.C. § 103(a) as being unpatentable over Petitou et al., U.S. Patent 5,378,829, essentially for the reasons set forth in the Office Actions in parent application Serial No. 09/202,241.

The Examiner maintains that Petitou teaches saccharides comprising the same disaccharide units as the instant claims, with the exception that the Petitou compounds may have at most 6 monosaccharide units, and that Petitou also teaches synthetic processes and

therapeutic methods for the smaller compounds which are completely analogous to those of the instant claims. The Examiner then urges that it would have been obvious for a person of ordinary skill in the art at the time of the invention to substitute saccharides as claimed comprising 8-24 monosaccharides for those of Petitou comprising 6 monosaccharides, and that an ordinarily skilled worker would have been motivated to do so because the claimed saccharides, like those of Petitou, comprise the crucial saccharide linkages for heparin activity. Thus, there would have been a reasonable expectation of success. The rejection is respectfully traversed and reconsideration thereof is requested.

As stated at page 2, lines 7-9, of Applicants' specification, the art at the time of the invention was directed to investigating therapeutically effective oligosaccharides of the lowest molecular weight possible. At the time, there was no method of synthesizing compounds of increased chain length (specification page 2, lines 18-19) and in fact, Petitou, itself being representative of the state of the art at the time of Applicants' invention, teaches away from long chain compounds and describes saccharides having at most six monosaccharide units. The advantage of the Petitou compounds is said to reside, not in the presence of saccharide linkages as is relied upon in the present Office Action, but in the absence of free hydroxy, N-sulfate and N-acetate groups (column 1, lines 29-32), which are replaced with alkyl, aryl, or aralkyl functionalized saccharide units, thereby improving the compounds' binding affinity, pharmacokinetics, dosing options, and simplifying their synthesis (column 1, lines 49-63). Nowhere does Petitou teach or even remotely suggest that the actual number of saccharide linkages or the distribution of the functional groups within the saccharide chain might have an effect on the compound's therapeutic efficacy or selectivity.

Contrary to the disclosure of Petitou, which explicitly limits the number of monosaccharide units to six, Applicants have surprisingly discovered that polysaccharides containing 8 or more saccharide units have biological activities that are not only selective, but also quantitatively high. Applicants have further discovered that the activity of these polysaccharide compounds may be quantitatively modulated according to the length of the saccharide chain and by the distribution of the functional substituents on the various units (specification page 2, line 31 to page 3, line 1).

As explained at page 3, lines 11-26, of the instant specification, Applicants have found that polysaccharides of 8-24 monosaccharide units formed from a sequence of disaccharides containing a uronic acid and a hexose wherein all the hydroxyl groups are etherified with a (C₁-C₆) alkyl group or esterified as a sulfate group and wherein each disaccharide is at least monoetherified, make it possible to modulate with precision the activities of the polysaccharides to obtain compounds of high activity and selectivity.

Thus, Applicants have surprisingly and unexpectedly found that increasing and specifying the length of the saccharide chain, as well as specifying the location of the particular functional substituents on the chain members, can provide an increased and selective therapeutic activity. Sulfated and alkylated decasaccharides, for example, can be potent selective inhibitors of bFGF according to the arrangement of the alkyl and sulphate groups; tetradecasaccharides can be selective inhibitors of factor Xa; and hexadecasaccharides can have a heparin-like activity, i.e., as much effect on factor Xa as on the thrombin (specification page 3, lines 2-10).

At the time of Applicants' invention, the art, as exemplified by Petitou, showed no recognition of the importance of the number of saccharide linkages, or of the distribution of

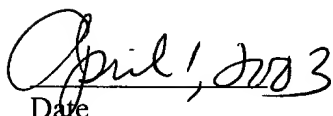
substituents within a polysaccharide chain, and was aimed at investigating compounds of the lowest molecular weight possible. Despite those teachings, Applicants have discovered that polysaccharides having at least 8 monosaccharide units, as herein described, can provide selective and improved activity over the compounds of the prior art. Only through hindsight, reconstruction in light of Applicants' own disclosure can the teachings of Petitou be modified to arrive at Applicants' claimed compounds.


Accordingly, it is submitted that at the time of Applicants' invention, the subject matter of the instant claims would not have been obvious to one of ordinary skill in the art. The rejection under 35 U.S.C. § 103(a) should therefore be withdrawn.

There being no remaining issues, this application is believed in condition for favorable reconsideration and such action is earnestly solicited.

A Notice of Appeal is submitted herewith.

Respectfully submitted,


Date


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